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A STUDY OF THE ACTION OF IODINE UPON GALLIC  
ACID AND ITS DERIVATIVES

BY

SOLOMON LEONARD FISHMAN

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THESIS

FOR THE

DEGREE OF BACHELOR OF SCIENCE

IN

CHEMICAL ENGINEERING

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Solomon Leonard Fishman

ENTITLED.....A Study of the Action of Iodine upon Gallic Acid

.....and Its Derivatives

IS APPROVED BY ME AS FULFILLING THIS PART OF THE REQUIREMENTS FOR THE

DEGREE OF.....Bachelor of Science in Chemical Engineering

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PART I. THE PREPARATION OF THE IODINE DERIVATIVES OF GALLIC  
ACID AND ITS METHYL AND ETHYL ESTERS.

1. Introduction.

The value of the halogens and of iodine especially as antiseptic agents has been well established. The use of iodine has been rather limited on account of its great cost and the limited methods of use. Thus we find tincture of iodine, a ten per cent alcoholic solution of iodine to be the universal method for utilizing iodine as an antiseptic. Iodoform and iodine trichloride are also used to a certain extent. The antiseptic action, which is defined as the power of a substance to kill pathogenic microorganisms, in all these compounds is due solely to the free iodine.

It has been known that a great variety of aromatic substances have marked antiseptic properties. Among these phenol and its derivatives are the best known. Keeping that in mind with what was said about iodine in the preceding paragraph, the logical conclusion was drawn that a phenolic compound in combination with iodine ought to have the additive antiseptic properties of both the iodine and the phenol. Gallic acid was taken as the phenol to be studied.

The problem then narrowed down to the preparation of the iodine derivatives of gallic acid and its ethyl and methyl esters, in which the iodine had replaced the two remaining hydrogen atoms in the benzene nucleus.

2. Historical Review of Literature.

There is little literature, if any at all, on the particular iodination involved in this paper. However, there appear to be a number of papers on the iodinations of analagous aromatic compounds which ought to be mentioned.

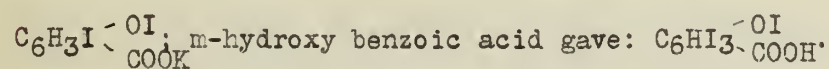


Ernst and Zwenger<sup>(1)</sup> prepared both the ethyl and methyl derivatives of gallic acid in 1871 by the following method.

Gallic acid was dissolved in absolute alcohol and dry hydrochloric acid gas was passed through the solution which had been heated to boiling. The esterification is almost a complete one if the hydrochloric acid gas is passed into the solution to the point of saturation and if alcohol is present in sufficient excess. The darkly colored fluid is then evaporated to dryness on the water bath, the dried mass is then broken up and heated for a time at 100 degrees C. The mass then should be carefully heated to its point of fusion to expel all the volatile matter, which prevents proper crystallization of the ethyl gallate. By taking up the ester with sufficient water to give a saturated hot solution and then allowing it to cool, ethyl gallate crystallizes out. Further recrystallization purifies the ethyl gallate.

In regard to the iodination, Classen and Löb<sup>(2)</sup> in 1895 obtained the tetraiodo derivative of phenolphthalein without the presence of free alkali. A borax solution of phenolphthalein was treated with a potassium iodide solution of iodine.

In 1889 Messinger and Vortmann<sup>(3)</sup> prepared the iodine derivatives of a number of phenols in the presence of potassium hydroxide. They found that phenol when iodinated gave diiodophenol iodide,  $C_6H_3I_2OI$ ; that o-, m-, and p-cresol gave similar compounds as with phenol; that thymol first gave a mono-iodide derivative and then a complex polymerized product; that resorcin gave a compound of the formula  $C_6H_2I_2\begin{smallmatrix} OK \\ \diagup \\ OI \end{smallmatrix}$ ; that guaiacol gave a derivative in between the mono and the diiodo substitution product; that o-hydroxy benzoic acid gave the potassium salt of diiod salicylic acid of the following formula:







Benedikt<sup>(4)</sup> in 1879 studied the constitution of the pentahalogen derivatives of resorcin and orcin and attempted to strike an agreement between the properties of these substances and their new formula.

Korner and Belasio<sup>(5)</sup> in 1908 iodinated m-nitroaniline by adding iodine dissolved in a 25% aqueous potassium hydroxide solution to a solution of the base dissolved in hydrochloric acid, containing potassium iodate; by using one molecule of iodine per molecule of base, a mixed product was obtained, containing the various iodine substitution products, which could be separated only with great care.

Wilkie<sup>(6)</sup> in 1912 observed that the addition of a drop of iodine to a saturated solution of sodium triiodophenol produced a striking color effect, the solution becoming semi solid, owing to the precipitation of tetraiodophenylenequinone.

Casanova and Carcano<sup>(7)</sup> in 1912 stated that when iodine acts on tannin (digallic acid) in the presence of water, the tannin molecule is partly oxidized into simpler derivatives, but no organic iodine compounds are formed, as the whole of the iodine is found to be transformed completely into hydriodic acid.

Becquet<sup>(8)</sup> in 1912 further states that tannin and iodine are not chemically combined; the tannin serves as a substratum for hydrogen iodide.

From the work of these various authors the following conclusions and inferences may be drawn:

1. That iodinations of organic compounds can be carried out in alkaline solutions.
2. That the iodination is specific for every compound.
3. That the derivative may be formed and decomposed immediately afterward by the presence of an excess of iodine.



4. That the iodine derivative of gallic acid and its methyl and ethyl esters may not be formed, but decompositions may result.

### 3. Methods found given in the literature.

Lassar-Cohen gives the following methods for the iodination of organic compounds in general:

1. Direct iodination.
2. Iodination by solution and by oxidizing agents.
3. Iodination in neutral and alkaline solution.
4. Iodination in acid solution.
5. Iodination in borax solution.
6. Application of iodine in a nascent state.
7. Addition of iodine to unsaturated compounds.
8. Iodination in presence of iodine carrying agents.
9. Other iodinating agents.
10. Introduction of iodine in place of bromine or chlorine.

As solvent agents for the iodine in the above processes, the following substances have been used:

borax solution	potassium iodide solution
chloroform	petroleum ether
glacial acetic acid	sulfur dioxide in aqueous solution

As oxidizing agents in the above processes the following have been used:

stannous oxide	mercuric oxide
iodic acid	nitric acid
sulfuric anhydride	

As iodination in an alkaline or in a borax solution seems to be the





most feasible on account of the completeness of the reaction and the high yields possible; as a consequence, examples of both these processes will be mentioned.

8.2 kilograms of eugenol  $\left[ \begin{array}{c} \text{OH} \\ | \\ \text{C}_6\text{H}_3\text{-OCH}_3 \\ | \\ \text{CH}_2\text{CH}=\text{CH}_2 \end{array} \right]$  were

dissolved in 700 liters of water. To this is added two kilograms of caustic soda and 2.7 kilograms of sodium carbonate. Upon adding a solution of 12-13 kilograms of iodine in 18 kilos of potassium iodide dissolved in 60 liters of water, the iodinated eugenol separates out abundantly. As the sodium carbonate has the function of removing hydriodic acid, sodium acetate or bicarbonate may be used in its place.

Classen obtained the tetraiododerivative of phenolphthalein in the following way: Twenty grams of phenolphthalein were dissolved in four liters of water, which contained borax in solution, and ninety grams of iodine in one hundred grams of potassium iodide and five hundred cubic centimeters of water were added to the warm solution.

Beilstein gives the following for the preparation of the ethyl ester of gallic acid:

One part of gallic acid is dissolved in four parts of 86% ethyl alcohol; the solution is heated to the boiling point and then saturated with hydrochloric acid gas; the resulting solution is then heated to a syrupy mass, and then barium carbonate, lime free, is added. The mass, after hardening, is extracted with absolute ether.

The crystals are irregular rhombic prisms, containing two and a half molecules of water, which escape at 100 degrees C. upon heating, and can be crystallized water free from chloroform. Upon rapid heating, the ethyl gallate melts at 90 degrees, the water free ester melts at 141 degrees, 150 degrees



or 158 degrees. It is slightly soluble in cold water, very soluble in hot water, in alcohol and in ether; very slightly soluble in boiling chloroform. It acts similarly as the free gallic acid does towards ferric chloride, gold and silver solutions. It decomposes into alcohol and pyrogallol upon dry distillation.

The method of Ernst and Zwenger<sup>(1)</sup> as given in the historical review was utilized also.

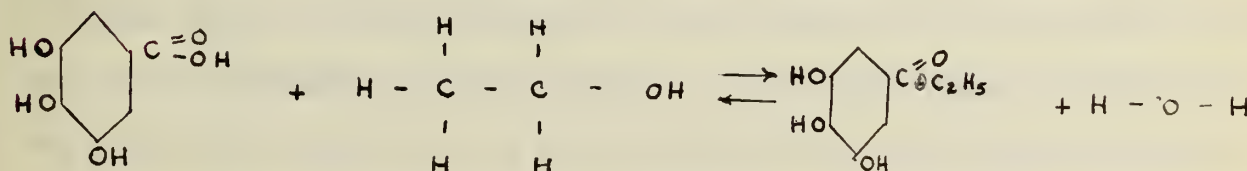
#### 4. Methods Employed in the Preparation of the Desired Compounds.

Preparation of the Ethyl and Methyl Esters of Gallic Acid. One hundred grams of gallic acid and four hundred grams of 86% ethyl alcohol were heated to the boiling point and a stream of dry hydrochloric acid gas was passed through the liquid. The solution was heated until it became viscous and barium carbonate was then added. The solid was then extracted with absolute ether and the ethyl gallate was crystallized.

The crystals obtained were long prisms which melted from 144-147 degrees and were readily soluble in water. The following table gives an idea of the results obtained:

Gallic acid	Ethyl alcohol	Theor. Yield	Act. yield	% yield	M.P.
100 gm.	400 gm.	117 gm.	55 gm.	47.2%	144-147° C.

The equations representing the reactions in the above operations are:







The preparation of the methyl ester of gallic acid was analogous to that of the ethyl ester, methyl alcohol being substituted for ethyl alcohol. Two hundred grams of methyl alcohol and fifty grams gallic acid were heated to boiling and hydrochloric acid gas passed into the hot liquid. After two hours the apparatus was disconnected and the solution evaporated to dryness. Water was found to be the best agent from which to crystallize the methyl gallate.

The results obtained can be summarized as follows:

Gallic acid	Methyl alcohol	Theor. Yield	Act. yield	% yield	M.P.
50 g.	200 g.	109 g.	70 g.	64.2	178

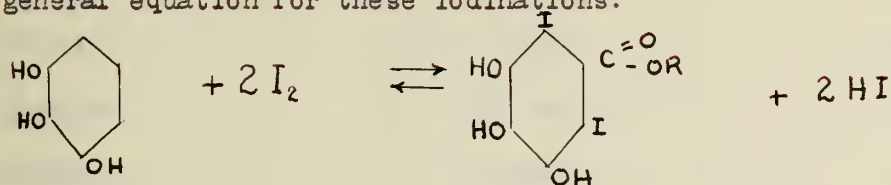
In iodinating gallic acid, four grams of gallic acid were dissolved in two hundred cubic centimeters of water in which twenty grams of borax had already been dissolved. Seventy five cubic centimeters of a solution containing sixteen grams of potassium iodide and fifteen grams of iodine were then added to the first solution which had been warmed. A darkly colored crystalline substance separated out. This substance which was supposed to be the diiod derivative of gallic acid, crystallized well from water and melted at 161°.

Sodium iodide was substituted for potassium iodide and was found equally satisfactory. Thirteen grams of sodium iodide were used in place of sixteen grams of potassium iodide.

In iodinating ethyl gallate, five grams of ethyl gallate were used in place of the four grams of gallic acid in the preceding directions. M.P. 175°. A similar amount of methyl gallate was used in place of the four grams of gallic acid in the iodination of methyl gallate. M.P. 178°. Water was found to be the best suited solvent for the recrystallization of the iodine derivatives of gallic acid and its ethyl and methyl derivatives. The following represents



the general equation for these iodinations:



Iodination in the presence of mercuric oxide was also attempted<sup>(9)</sup>.

Ten grams of gallic acid were dissolved in boiling methyl alcohol, the solution was slightly cooled and then a mixture of twenty seven grams of iodine and fifteen grams of mercuric oxide was gradually added. The solution was then heated to the boiling point and then filtered. The crude diiodo gallic acid crystallized out and this was freed from mercuric oxide by dissolving in cold chloroform and then further purified by crystallization from ethyl alcohol. Its melting point was found to be 162°-200°.

### 5. Results and their interpretation.

Fair yields were obtained in the preparation of ethyl gallate by the method described in the preceding section. The use of barium carbonate was found to be unnecessary, because equally as good, if not better, results could be obtained without it. The function of the barium carbonate evidently was to react with the hydrochloric acid in the solution, in order to prevent decomposition of the desired compounds.

The crystallization of the ethyl gallate was a rather difficult procedure, due, perhaps, to the hydrolysis of ethyl gallate to gallic acid. A series of solubility tests were made and the results are given in tabulated form:





Solvent	Cold	Hot
Water	sl. sol.	sol.
$C_2H_5OH$	sl. sol.	sol.
$(C_2H_5)_2O$	soluble	soluble
$CHCl_3$	insol.	insol.
$CCl_4$	insol.	insol.
Benzine	insol.	sl. sol.
Benzine	insol.	sl. sol.
Ligroin	insol.	sl. sol.
Petrol ether	insol.	insol.

By dissolving crude ethyl gallate in ether and then precipitating it by adding petrol ether, it was found that the best form and yield of crystals could be obtained.

Equally good results were obtained in the preparation of methyl gallate. Water was the best crystallizing agent.

The similarity of melting points and of crystallizing properties, in addition to the appearance of the solutions, lead to a suspicion that the ethyl and methyl gallates were hydrolyzed to gallic acid during the process of iodination and hence formed diiod-derivatives similar to those of gallic acid. In order to throw light upon this suspicion, several tests were undertaken.

The first test was the determination of the amount of iodine in the diiod gallic acid compound by the Carius method. Theoretically there should be 60.15% iodine in this compound. In one sample, 2.39% iodine was found, while in another, .293% iodine was present. Hence the compound prepared was not the diiodo derivative of gallic acid.

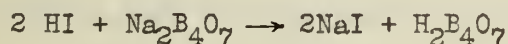
The melting point of each of the substances prepared was taken and



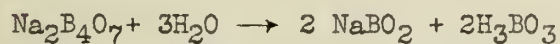
then the melting points of the mixtures observed. Diiodo gallic acid melted at  $162^{\circ}$ , while a mixture of diiodo gallic acid and diiodo methyl gallate gave a melting point of  $175-176^{\circ}$ . Diiodo ethyl gallate (M. pt.  $176^{\circ}$ ) and diiodo methyl gallate (M. pt.  $162^{\circ}$ ) gave a mixture melting at  $176^{\circ}$  on two checks.

On heating what was supposed to be diiodo gallic acid on a platinum foil, no burning took place. A dark residue resulted which, when leached with water, reacted acid with litmus. The compound was found to be very soluble in 5% caustic soda solution. When heated with copper oxide and when the resulting gases were passed through lime water, no clouding took place, which indicated that very little carbon, if any at all, was present in the compound.

In the preparation of all these compounds, the iodination took place in the presence of borax. The reaction that took place can be represented in this way:



Borax in concentrated aqueous solutions hydrolyzes in this way to give boric acid:



Boric acid has a melting point of  $185^{\circ}$ ; it is slightly soluble in cold, very soluble in hot water. Considering the tests made on the compounds that were prepared, and the properties of boric acid, it must be admitted that the compounds obtained were nothing else but an impure boric acid.

The iodination of gallic acid was also attempted in the presence of mercuric oxide. The melting point of the crude residue was  $229^{\circ}$ . The crystals obtained were darkly colored and on standing became darker, iodine evidently dissociating.





## 7. Summary.

From these various results, it may be concluded that:

1. The preparation of the diiodo substitution derivatives of ethyl and methyl gallate in aqueous solution of borax was found to be impossible on account of the hydrolysis that took place during the iodination.
2. That the iodination of gallic acid and its methyl and ethyl esters in the presence of borax was accompanied by a hydrolysis of borax to boric acid, that the latter substance crystallized out and was mistaken for the desired compound.
3. That the iodination of gallic acid in the presence of mercuric oxide was unsatisfactory because the resulting crystallized product decomposed rapidly, as was shown by melting point determinations.
4. That the results agree with what might be expected from an analogy from the work in 1889 of Messinger and Vortmann<sup>(3)</sup> on the iodination of phenols.
5. That the iodination cannot be carried on successfully by any direct method such as was used in this work.



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PART II. P-HYDROXY PHENYL ETHYL DIMETHYL AMINE AND  
P-HYDROXY PHENYL ETHYL AMINE.

1. Introduction and Historical Review  
of the Literature.

The therapeutic value of p-hydroxyl phenyl ethyl dimethyl amine was first studied by E. Leger. He obtained it from the malt dust of barley as a new alkaloid and called it hordenine. The extract was obtained in ether, the ether was evaporated off, and the resulting mass was crystallized and then further purified with alcohol.

E. Leger further states that hordenine forms colorless, almost tasteless anhydrous prisms, fusible at  $117^{\circ}$  to a colorless liquid. If it is maintained at this temperature for a long time or better at  $140-150^{\circ}$ , it volatilizes and can be sublimed similarly to camphor, without any sensible alteration. Its alcoholic solution is without action on polarized light; the aqueous solution of the sulfate salt acts similarly.

Hordenine is dissolved readily in alcohol, in chloroform, in ether and can be crystallized from these different solvents. It is dissolved with difficulty in toluene and is still less soluble in commercial xylene. Its solubility in petroleum ether in the cold is very slight.

Hordenine is a strong base, which not only blues red tornesol, but also reddens phenolphthalein and loses ammonia in the cold. Sulfuric acid does not concentrate its color; it is strongly attacked by a concentrated potash solution. On the other hand it is oxidized by potassium permanganate in acid solution and on heating this with ammoniacal silver nitrate and iodic acid, the iodide salt is precipitated.



The composition of hordenine corresponds to the formula  $C_{10}H_{15}NO$ . It is isomeric with ephedrine. In general it is very soluble in water. The following salts were prepared:

Sulfate  $(C_{10}H_{15}NO)_2 SO_4H_2 + H_2O$

Chlorhydrate  $C_{10}H_{15}NO.HCL$

Bromhydrate  $C_{10}H_{15}NO.HBr$

Iodohydrate  $C_{10}H_{15}NO.HI$

Iodomethylate  $C_{10}H_{15}NO.CH_3I$

Acetylhordenine  $C_{10}H_{14}(C_2H_3O)NO$

Iodohydrate of acetyl hordenine  $C_{10}H_{14}(C_2H_3O)NO.HI$

From these the author was able to conclude that the nitrogen in hordenine was tertiary and that the oxygen existed in the molecular as part of a hydroxyl group.

It was observed that the bacillus cholera could not develop in a broth of malt dust.

A continuation of Leger's studies by Camus (2) on the degree of toxicity and the symptoms of intoxication of hordenine led to the following results:

Hordenine sulfate was found to be a slightly toxic substance; when injected in a strong dose, it commonly gave the manifestations of ordinary cortical or bulbar. When death was produced it was determined by an arrest of the respiration. If the animal survived after having been strongly intoxicated, it recovered rapidly and completely in a few days.

Barger attempted to prepare hordenine by treating p-hydroxy phenyl ethyl amine with methyl iodide. The methyl iodide salt was obtained, but it was found impossible to isolate the alkaloid itself.





A suitable material for the synthesis of hordenine was, however, found in phenyl ethyl alcohol, a commercial product, from which chloro- phenyl-ethane could be prepared. The latter substance yielded with dimethyl amine the desired dimethyl amino phenylethane. After nitration of this tertiary base, the p-nitro compound was isolated as the oxalate. It was also found possible to obtain pure chloro p-nitrophenyl ethane by distillation and crystallization, and then to combine it with dimethylamine. On reduction the separation of the amino compound from the unchanged nitro compound proved difficult, since both substances are bases; the crude reaction product was therefore diazotized, and finally yielded a small quantity of a base, identical with the hordenine prepared from malt germs.

K. W. Rosenmund (4) in 1910 confirmed the results of Barger.

## 2. Methods Available for These Syntheses.

Rosenmund's method (4) for preparing p-hydroxy phenyl ethyl amine by first preparing nitrostyrol from anisaldehyde and nitromethane and then reducing nitrostyrol to the oxime with zinc dust and acetic acid, finally reducing the oxime to the amino compound is the best method, by far, for preparing this compound and was therefore used.

For the preparation of p-hydroxy phenyl ethyl dimethyl amine, the method given by Rosenmund (4) was found best suited. In this anisol and chloracetylchloride were allowed to react in the presence of aluminum chloride and chloranisolketone obtained. This was then treated with dimethylamine and then with dilute hydriodic acid, the hydrogen iodide salt of the p-methoxyphenylethyl dimethyl amine being obtained.

## 3 and 4. Experimental Work and Interpretation of Results.

45 gm. of anisaldehyde and 21 gm. of nitromethane were dissolved in



70 cc. of absolute alcohol, the whole mixture was kept cooled to  $0^{\circ}$ . To this solution was added 45 grams of 50% potassium hydroxide in 60 cc. of alcohol in small quantities, so as to keep the temperature of the mixture from rising above  $5^{\circ}$ . A potassium salt of nitrostyrol separated out during the operation and towards the end of the reaction the entire mass solidified. Upon addition of ice and 300 cc. of water a solution was obtained, which was then poured into an excess of hydrochloric acid and cooled by ice, whereby the para-methoxy-a-nitrostyrol separated as a yellow powder. This was then filtered off, washed with water and recrystallized from a small quantity of alcohol. The nitrostyrol separated in thin, intensely yellow crystals about two or three centimeters in length. The yield of the pure, crystalline compound amounted to about 40 gm., which is quantitative. This yield was obtained on two separate preparations of the compound. Its melting point was found to be  $87:88^{\circ}$ .

#### Direct Reduction of Nitrostyrol.

10 gm. of nitrostyrol and 5 gm. zinc dust were added to a mixture of 1 part glacial acetic acid and 3 parts alcohol in small portions, whereupon the solution was decolorized on strong heating. It was then filtered and 250 g. of 3% sodium amalgam were added, the reduction to amine following. In the operation sodium acetate separated out and was brought into solution by careful addition of water. When all the amalgam was used, the solution was diluted with twice its volume of water, the solution was shaken with ether to separate the unchanged oxime, and the bases formed were removed with strong caustic soda solution. The aqueous solution was shaken with ether; the combined extracts were dried over potassium carbonate and then concentrated. The bases and remaining behind were dissolved in acetone, upon cooling were treated with alcoholic hydrochloric acid in slight excess.





The hydrochloric acid salt of the base then should separate out in pure white plates of m. pt.  $205^{\circ}$ . In the number of attempts in this experiment to reduce the nitrostyrol, it was found impossible to obtain this hydrochloride salt. On that account, it was impossible to proceed further in the preparation of p-hydroxy phenyl ethyl amine.

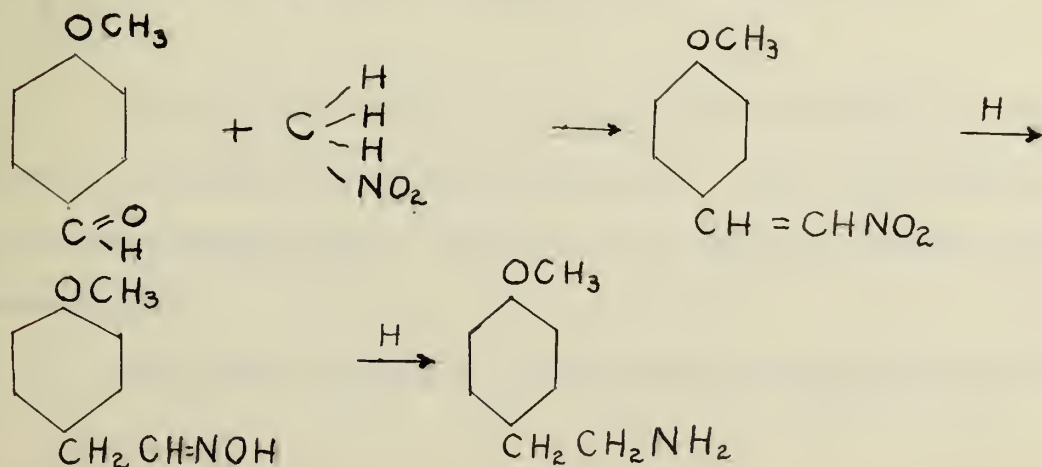
#### Reduction of nitrostyrol to p-methoxy phenyl ethyl oxine.

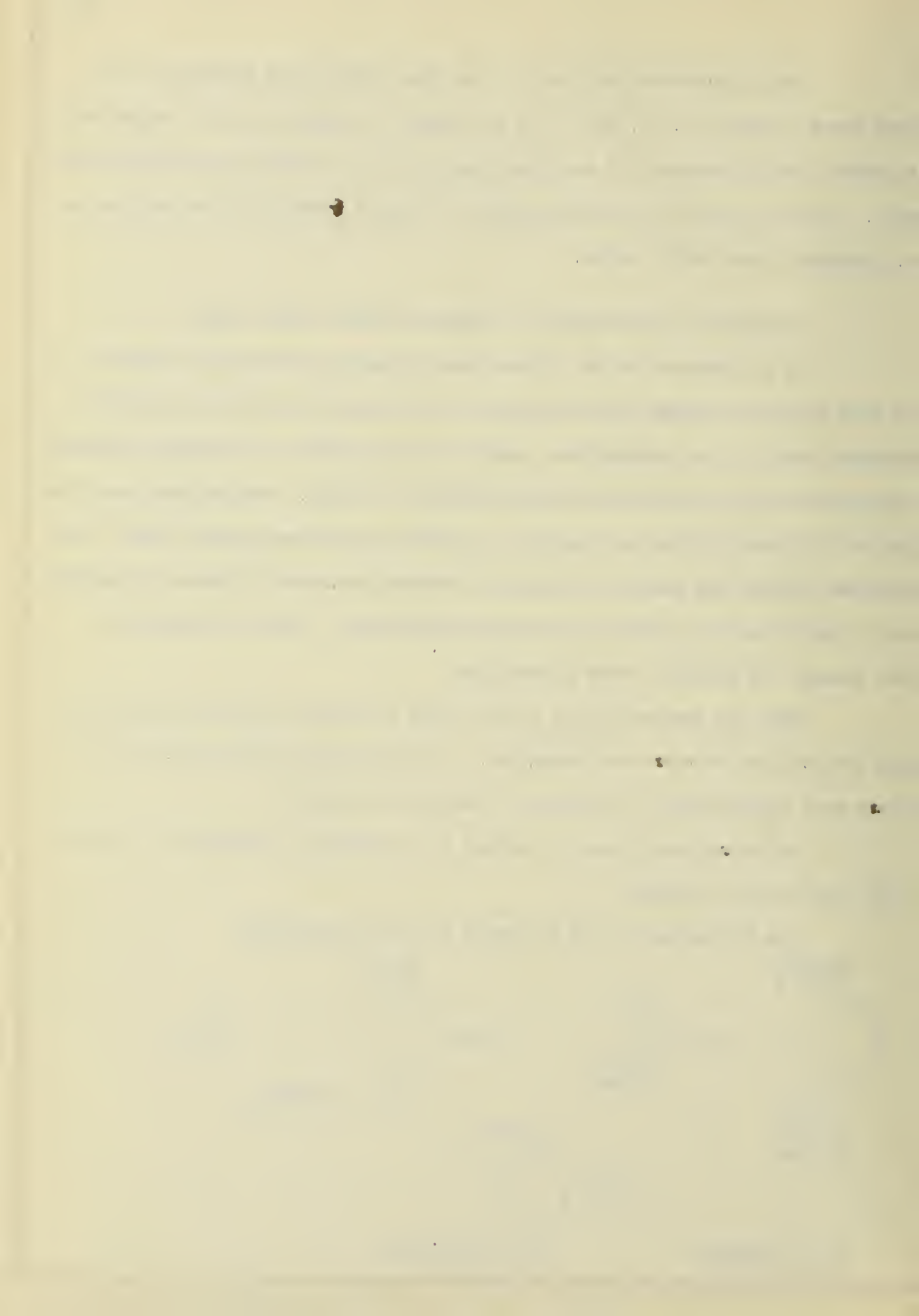
To a mixture of 70 gm. alcohol and 30 parts acetic acid a mixture of five grams nitrostyrol and four grams of zinc dust which had been suitably dampened with a little alcohol was added in small portions. Upon strong heating the yellow color of the nitro compound turned to a black. The solution was then cooled, filtered, diluted with water, and shaken with ether several times. The ethereal extract was shaken with sodium carbonate solution to remove the acetic acid, then dried over sodium sulfate and concentrated. After an interval in the vacuum, the residue became crystalline.

This was treated with a little ether to separate the oily by-product and the undissolved oxine was separated. On the average about 2.2-1.5 gm. of oxine were obtained from five grams of the nitro compound.

The oxine could then be reduced to the amine as indicated in the outline for direct reduction.

The following are the equations for these reactions:

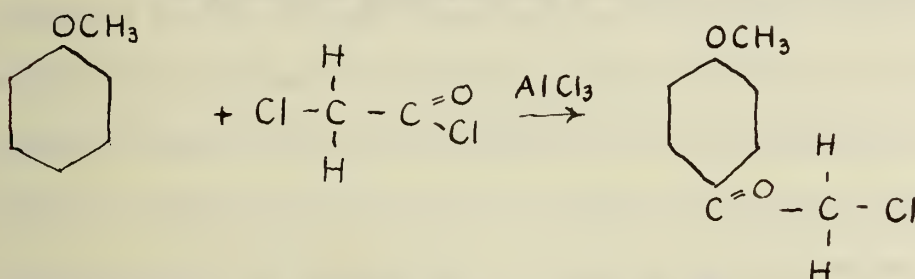




### Preparation of p-hydroxy phenyl ethyl dimethyl amine.

15 gm. of anisol and 22.5 gm. of chloracetyl chloride were diluted with carbon disulfide and 22.5 gm. of powdered aluminum chloride were added. The liquid separated into two layers, the upper colored red-yellow, the lower, dark red. The dark red, viscous mass was decomposed with water, throwing down a gray, easily crumbled mass, from which upon recrystallization from alcohol, white needles separated, about a centimeter in length, melting at  $102^{\circ}$ .

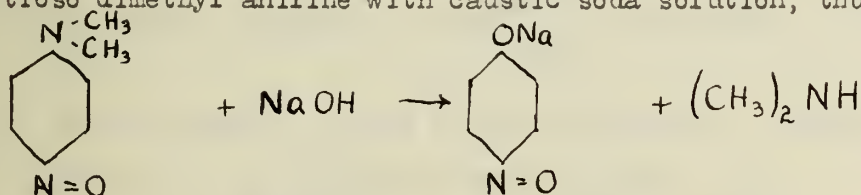
The equations representing the above reactions are:



### The Preparation of Dimethylamine.

Dimethylamine is a gas at ordinary temperatures, hence its direct preparation is not feasible. The hydrochloride salt seems to be the commonest form into which it is made, as this salt crystallizes well.

The old method for making dimethylamine hydrochloride was to treat nitroso dimethyl aniline with caustic soda solution, thus:



This dimethylamine was then passed into hydrochloric acid, from which the hydrochloric acid salt crystallized. This method involved the use of nitroso dimethyl aniline, which was quite expensive, and the yields were somewhat low.

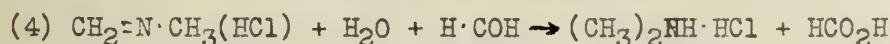
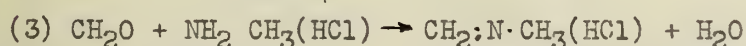
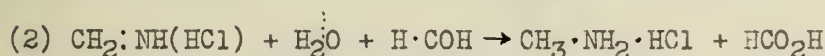
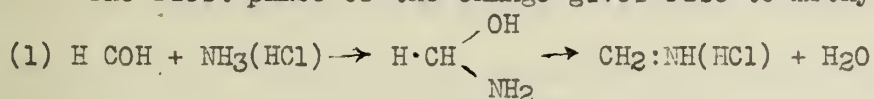
The method by which the dimethylamine hydrochloride was obtained





was by that given by Werner (5). Formaldehyde and ammonium chloride were heated in a flask for several hours at a temperature not above  $104^{\circ}$  and the volatile matter distilled. After cooling the liquid, and separating the crystallized ammonium chloride, the solution was heated again with 300 gm. of formaldehyde, using  $115^{\circ}$  as the maximum temperature and maintaining the reaction mixture at this temperature until no more liquid distilled. This required about four hours. The product was concentrated at  $100^{\circ}$  until a scum appeared on the surface of the hot liquid; upon cooling, the ammonium chloride and the methyl ammonium chloride were filtered off. The filtrate was then heated to  $120^{\circ}$ , until a portion when cooled became a semi-solid, crystalline mass, after which it was allowed to remain for two days in a partial vacuum over sodium hydroxide. This was then treated with chloroform and impure dimethyl amine hydrochloride obtained therefrom, as the ammonium chloride and the methyl ammonium chloride are not soluble in chloroform. This impure produce was then treated directly with caustic soda and the dimethyl amine gas absorbed in alcohol. The following reactions and table of various preparations made will simplify matters somewhat:

The first phase of the change gives rise to methylene imine, thus:



#### Results of Preparations.

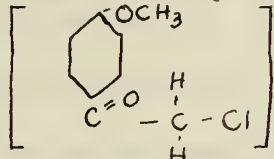
	1 Amt. of CH <sub>2</sub> O	2 Amt. of NH <sub>4</sub> Cl	3 Temp.	4 Time	5 Amt. of CH <sub>2</sub> O	6 Temp.	7 Time	8 Weight impure 4el. salt
1st Attempt	200	400	$104^{\circ}$	4 hrs.	300	$115^{\circ}$	4 hrs.	110
2nd "	200	400	104	4	300	115	4	



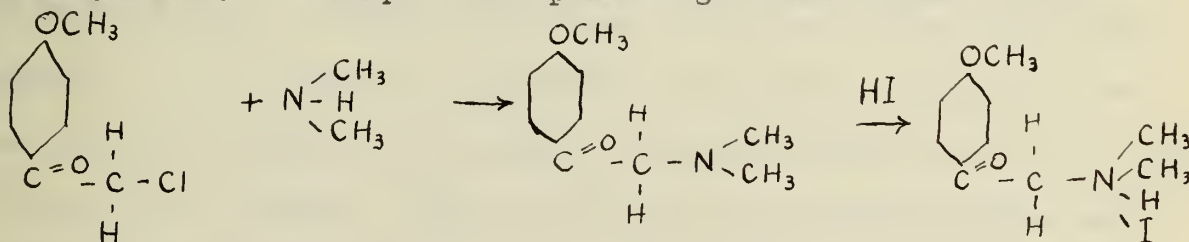


	Weight of $(\text{CH}_3)_2\text{NH}$ in alcohol in gms.	% yield
(Cont.) 1st attempt	60.8	36.2
2nd attempt	163	95.8

Preparation of p-methoxy phenyl athanon dimethylamine

12 gm. of chloranisolketone  and twenty

grams of a 33% alcoholic dimethyl amine solution were shaken in a sealed vessel until all the solid matter went into solution. This was then allowed to stand over for twenty four hours and was then evaporated in an open dish for 24 hours in a vacuum at room temperature, in order to separate the excess dimethyl amine. After acidifying with strongly diluted hydriodic acid, it was filtered, then shaken with blood charcoal, filtered once again and evaporated on the water bath to a syrupy consistency. The mass that was obtained in this way became crystalline on cooling and gave, after pressing and several recrystallizations from water, colorless crystal prisms, of the composition:  $\text{CH}_3\text{O}$   $\text{C}_6\text{H}_4\text{CO}$   $\text{CH}_2\text{N}(\text{CH}_3)_2\text{HI}$ . This melted at  $150^\circ$ . The yield amounted to 62% of the theoretical. The free base forms an oil, which solidifies in a cold mixture and melted at  $30^\circ$ . The equations representing the above reactions are:



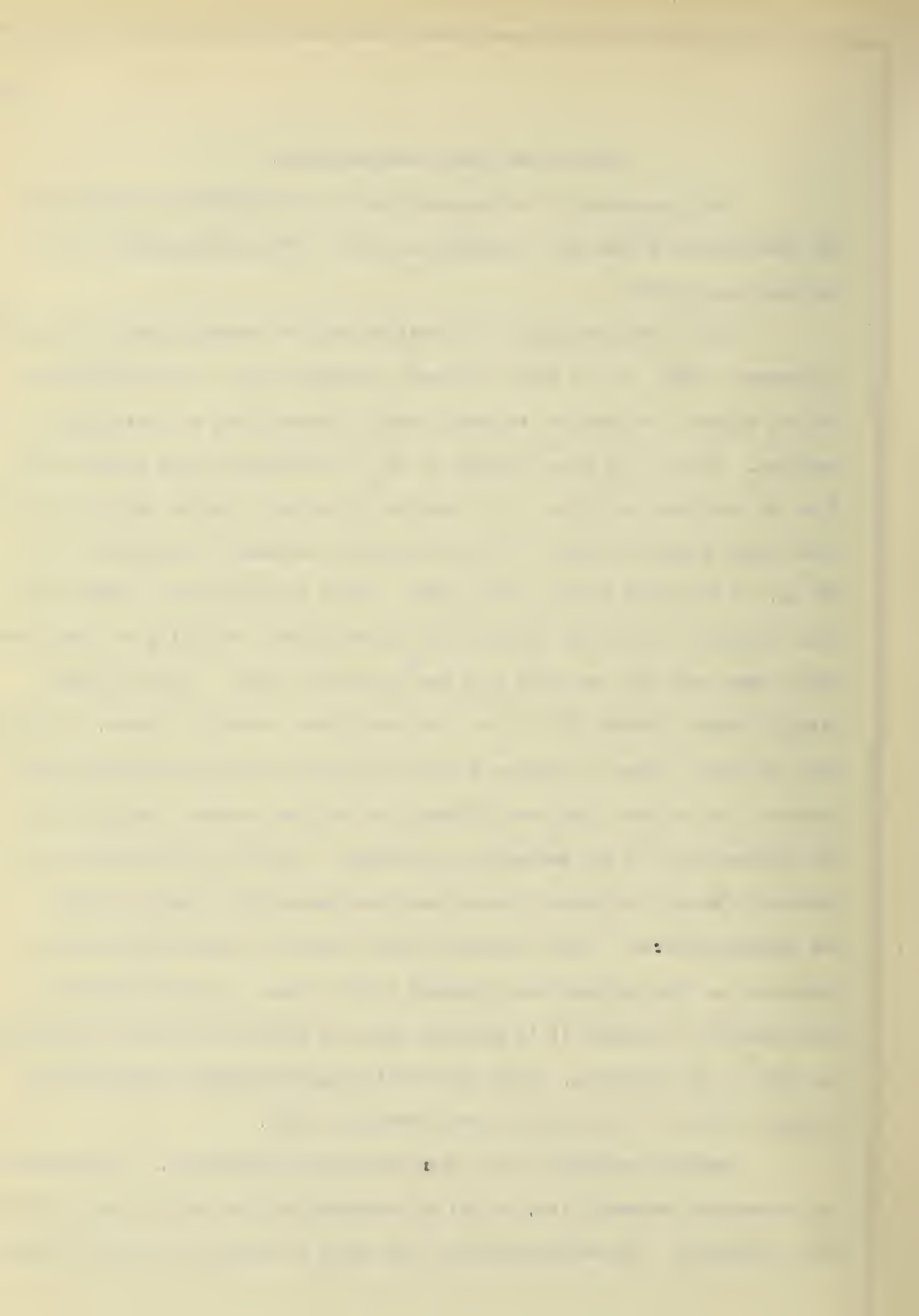


### Results and Their Interpretation.

The preparation of nitrostyrol was very successfully accomplished and quantitative yields were obtained each time. The melting point of the crystals was 87-88°C.

The direct reduction of nitrostyrol was not accomplished successfully on several trials, as the final substance described fully in the directions did not appear, the material evidently having entered into an intermediate reaction. Thus in the first attempt 10 gm. of nitrostyrol were reduced with 8 gm. of zinc dust in 100 cc. of a mixture of one part glacial acetic acid to three parts absolute alcohol. This mixture was refluxed, filtered and to it 200 gm. of 3% sodium amalgam, were added. After the reduction to amine was about complete, the sodium acetate that separated out, according to directions, should have gone into solution upon the addition of water. The more water actually added, however, the denser the precipitate seemed to become. Finally when the water seemed to have no effect on bringing the suspended matter into solution, the entire liquid was filtered and the free mercury resulting from the decomposition of the amalgam was recovered. The clear liquid was now diluted with twice its volume of water and then shaken with ether to remove the unchanged oxime. Strong, caustic soda solution was added, but no base separated, so the solution was discarded at this point. As the directions were carefully followed, it is possible that the difficulty lies in some particular step in the reduction. Thus the solution upon refluxing becomes darkly colored, instead of colorless as the directions state.

Partial reduction to the oxime was more satisfactory. The yields of the oxime were extremely low, as the oil accompanying the product was separated with difficulty. The melting point of the oxime was found to be in the range





from 110 to 130°, whereas the literature gives 120°. Evidently some oil still was present with the oxime when the melting point was taken.

As time did not permit, further work was not carried on beyond this particular compound.

The preparation<sup>of</sup> chloranisol ketone was one that gave good results. Using 15 gms. of anisol and 22.5 gm. of chloracetchloride, about 12 gm. of the ketone were obtained. Theoretically 25.6 gm. should have been obtained. Hence the yield was 46% of the theoretical. The melting points of the different preparations were about the same; 95°, 101°, 102°; the latter being the nearest to the correct value.

The preparation of dimethyl amine from ammonium chloride and formaldehyde was an entirely successful one. Although the yield in the first attempt at its preparation was rather low, that in the second attempt was much more satisfactory, amounting to about 95%. The dimethyl amine was regenerated by dropping the aqueous solution of the hydrochloride salt of dimethylamine on a concentrated caustic soda solution and then bubbling the gas through alcohol. In this way a strong solution of the gas in alcohol was obtained.

p-Methoxyphenyl athanon dimethyl amine hydrogen iodide was obtained in the form of yellow crystals melting in the vicinity of 150°, but not exactly at 150°, indicating the presence of some impurity.

The results in tabular form are:

Wt. of chlor anisol ketone	Wt. of dimethyl amine	Wt. of product	Theor. Yd.	Pctge. Yd.	M.P.
12 g.	7.35 g.	2 g.	12.6 g.	15.9	149.0

The yields were poor, making it difficult to obtain sufficient hydrogen iodide compound with which to work further and it is upon this point that the author is now busy.



### 5. Conclusion and Summary.

From these preparations, studies and observations, the following conclusions may be drawn.

1. That nitrostyrol can be prepared very readily from styrol and nitro methane.
2. That the nitrostyrol cannot be satisfactorily reduced directly; that reduction to the oxime undoubtedly takes place, since the oxime could be isolated and identified.
3. That chloranisol ketone can be readily prepared from anisol and chloracetyl chloride by the Friedel and Crofts' reaction.
4. That dimethyl amine can be prepared very satisfactorily and cheaply from ammonium chloride and formaldehyde.
5. That the preparation of methoxy phenyl athanon dimethyl amine hydrogen iodide could be prepared by the interaction of chloranisol ketone and dimethyl amine.



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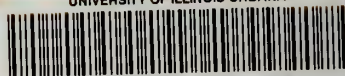
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